*REMARKS*

In the Office Action mailed February 12, 2003, the Examiner rejected claims 7-18 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 7 and 14-18 were rejected under 35 U.S.C. § 102(b) as being anticipated by Schoolnik et al. (U.S. Patent No. 4,777,239) and claims 7 and 14-18 under 35 U.S.C. § 102(b) as being anticipated by Breitburd et al. (WO 8701375, 1987). In addition, the Examiner rejected claims 7-18 under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Dillner et al (WO 91/18294).

By this paper, claims 7-10, 14, 17 and 18 have been amended to more particularly point out and distinctly claim the novel subject matter of this invention. In addition, claims 1-6, 15 and 16 have been canceled, without prejudice, and claims 19-22 have been added. Thus, following amendment by this paper, claims 7-14 and 17-22 are presented for examination. For the reasons set forth below, these claims are believed to be in condition to allowance. Favorable reconsideration of the application, as amended, and in view of the following remarks is respectfully requested.

In response to the rejection of claim 7 under 35 U.S.C. § 112, second paragraph, Applicant contends that the term "derived" is not a relative term and that no further definition is required as it would be obvious to one of skill in the chemical and biological arts to know that "derived" means "to produce or obtain (a compound) from another substance by chemical reaction" (*See*, The American Heritage® Dictionary of the English Language, Fourth Edition, Houghton Mifflin Company, http://dictionary.reference.com/search?q=derived accessed 4/30/03) and "to obtain (a chemical substance) actually or theoretically from a parent substance." (*See*, Merriam-Webster On-Line Dictionary; Merriam-Webster Inc., http://www.m-w.com/cgi-bin/dictionary accessed 07/14/03).

However, in an effort to further conform with the Utility Examination Guidelines, Applicant has amended claims 7 and 14 by substituting the word "isolated" for the word "derived." (*See*, 66 Fed. Reg. 1092, 1093 (2001)). Applicant contends that these terms have the same meaning in the art, therefore the replacement of the word "derived" with "isolated" sufficiently addresses the Examiner's rejection.

In response to the Examiner's rejection of claim 7 under 35 U.S.C. § 112, second paragraph, directed to omitting essential elements, Applicant contends that peptides that are reactive with antibodies are defined in the specification as "antigenic." (*See*, Substitute Specification at page 1, paragraph 1). Applicant assets that claim 7 is directed specifically to antibodies from peptides derived from the E2 early coding regions of human papillomavirus strains 16 and 18 and therefore is complete with regard to the individual claim elements.

Responsive to the Examiner's rejection of claim 9 under 35 U.S.C. § 112, second paragraph, Applicant has amended claim 9 to reflect that carboxymethlycysteine is substituted for one or more of the cysteine residues in the sequence. Applicant contends that the rejection to claim 9 is overcome with the new amendment since it is not necessary to specify which cysteine residue is being substituted for, therefore whether the cysteine is closer to the carboxyl terminus or the amine terminus is not relevant to the recited claim limitation.

In response to the Examiner's rejection of claim 10 under 35 U.S.C. § 112, second paragraph, Applicant suggests there may exist some confusion on the part of the Examiner about the subject matter being claimed by Applicant. Applicant's invention is a diagnostic method directed to detection of infection and/or cellular abnormalities (*i.e.*, koilocytosis, hyperkeratosis, precancerous conditions encompassing intraepitlehial-lesions, high-grade dysplasias, and invasive or malignant

cancers). (*See*, Substitute Specification at page 8, paragraph 23). Applicant's specification also teaches that "[i]t is a still further object to provide a simple, rapid, less expensive and more sensitive test for diagnosing not only HPV infections, but also most, if not all, HPV associated neoplasms." (*See*, Substitute Specification at page 4, paragraph 9). Moreover, Applicant has added claims 20 and 21 which further define the term cervical cellular abnormalities. Consistent with the foregoing, Applicant asserts that the Examiner's rejection of claim 10 under 35 U.S.C. § 112, second paragraph has been overcome by the support contained in the specification.

In further response to the Examiner's rejection of claims 10-13 under 35 U.S.C. § 112, second paragraph, claim 10 has been amended to more clearly define that an epitope is being detected and not an infection. In addition, Applicant has added claim 22 which further defines the word "epitope." Thus, detection of an HPV epitope is an object of the method and not detection of an HPV infection.

In response to the Examiner's rejection of claims 11-13 under 37 CFR 1.75(c), claim 7 has been amended to include the diagnosis of cervical disease or detection of cervical cellular abnormalities. It is submitted, therefore, that newly amended claim 7 overcomes the Examiner's rejection under 37 CFR 1.75(c).

In addition, Applicant refers the Examiner to the argument hereinabove directed to the use of the word "derived" in response to the Examiner's rejection of claims 14-16 under 35 U.S.C. § 112, second paragraph. Applicant has amended claim 7 and 14 by substituting the term "isolated", in accordance with the Utility Examination Guidelines, for the term "derived."

Based on the foregoing, Applicant notes that claims 7 and 9-14 have been amended to either provide clear antecedent basis for each of the terms identified by the Examiner or to include a

recitation of the relationship between elements, as requested by the Examiner. It is submitted, therefore, that the rejections under 35 U.S.C. § 112, second paragraph, have been overcome.

In rejecting claims 7 and 14-18 under 35 U.S.C. § 102(b), the Examiner asserts that Schoolnik et al. teaches the use of human papillomavirus (HPV) peptide in a diagnostic assay (*See*, column 4, lines 53-57, and column 9 lines 59-68), tissue type (*See*, column 10, lines 14-18), and with respect to HPV E2, E6, E7 protein (*See*, claim 1).

In rejecting claims 7 and 14-18 under 35 U.S.C. § 102(b), the Examiner asserts that Breitburd et al teaches the use of E7, E6 peptides for *in vitro* diagnostic assay to determine infection in a sample and teaches the raising of antibodies against the peptides (*See*, all the claims).

In rejecting claims 7-18 under 35 U.S.C. § 102(b) and 103(a) as being anticipated by or, in the alternative, obvious over Dillner et al (WO 91/18294), the Examiner asserts that Dillner et al discloses a method of detecting the presence of human papillomavirus for detecting the immune, including, cervix cancer and carcinoma (*See*, the abstract, and claims 1-9). The Examiner also asserts that one of ordinary skill in the art would have been highly motivated by the teaching of Dillner et al to delete one amino acid from the sequence already taught by Dillner et al (*See*, page 38, line 5), which reads on the SEQ ID NO: 1 of the applicant and differs by one amino acid, to be utilized in a detection assays for detection of serum antibodies against papillomavirus antigen. The Examiner further asserts that one of ordinary skill in the art being familiar with the above cited art would not have anticipated any unexpected results, and none have been provided. The Examiner further maintains the cited art taught the peptide as well as a method of detecting.

In response to the Examiner's rejection of claims 7 and 14-18 under 35 U.S.C. § 102(b), as being anticipated by Schoolnik et al., Applicant asserts that the defense of anticipation is improper because the prior art reference does not identically disclose every element or feature of the claimed invention as arranged or connected together as specified in the newly amended claims. More specifically, Schoolnik et al. does not disclose a peptide sequence which overlaps any of the amino acids specified in SEQ ID NO: 1. On the contrary, Schoolnik et al. teaches a series of seventeen (17) synthetic peptides as useful in diagnosis and therapy of conditions associated with HPV infection. Schoolnik et al. further discloses the use of the peptides to detect the presence of antibodies raised against HPV.

In response to the Examiner's rejection of claims 7 and 14-18 under 35 U.S.C. § 102(b) as being anticipated by Bretiburd et al., Applicant contends that Breitbard et al. teaches the use of diagnostic kits containing antibodies directed to the L2 genes of different papillomaviruses. There does not appear to be any specific mention of E2 early coding regions. In addition, there does not appear to be any teaching that discloses the use of diagnostic kits for detecting infection with specific HPV strains and for specific pathologies, such as cervical dysplasias (*i.e.*, cervical cancer).

In response to the Examiner's rejection of claims 7-18 under 35 U.S.C. § 102(b) and 103(a), as being anticipated by or, in the alternative, obvious over Dillner et al, Applicant contends that Dillner et al. teaches a method for diagnosing the presence of HPV infection and papillomavirus carrying tumors by immunoassay targeted to forty-one (41) specific peptide sequences. Moreover, these sequences are drawn from specific HPV strains and early coding regions. The Examiner asserts that it would be obvious to one skilled in the art and it would not be undue experimentation to cleave one peptide and arrive at Applicant's invention. Applicant disagrees.

Dillner et al. teaches an invention directed to specific sequences within specific strains of HPV including, 1, 5, 6, 8, 11, 16, 18, 31, 33 and 56. Dillner et al. suggests that minor modifications may be made to these sequences without departing from the invention. However, Dillner et al. teaches away from the assertion that minor modifications may be made to arrive at the Applicant's invention. In particular, Dillner et al. teaches that "[i]t is not at all obvious that immunoreactive regions of the other HPV viruses should be located within the same relative regions, and as can be seen below, the successful discovery of immunoreactive regions have been very different for different peptides and different HPV types." (*See*, Dillner et al, page 2, lines 16-20.)

In contrast, Applicant teaches a diagnostic method directed to detection of infection and/or cellular abnormalities (*i.e.*, koilocytosis, hyperkerotosis, precancerous conditions encompassing intraepitlehial-lesions, high-grade dysplasias, and invasive or malignant cancers). (*See*, Substitute Specification at page 8, paragraph 23). Applicant's specification also teaches that "[i]t is a still further object to provide a simple, rapid, less expensive and more sensitive test for diagnosing not only HPV infections, but also most, if not all, HPV associated neoplasms." (*See*, Substitute Specification at page 4, paragraph 9). Moreover, the present invention teaches that "[c]ancers stem overwhelmingly from HPV 16 and 18, but also from types 31, 33, 35, 45, 51, 52, 56 and 58. The virus infects cervical and other cells that can support virus propagation, where it causes abnormal cellular changes that can lead to life-threatening malignancies." (*See*, Substitute Specification at page 2, paragraph 2). Thus, Applicant teaches at least five (5) additional HPV strains that were not previously taught in Dillner et al. In further contrast, Dillner et al. specifically teaches that it is not obvious that there would be homology between immunoreactive regions in HPV strains.

As the foregoing demonstrates, none of the references cited in the Office Action, either alone or in combination, teach, disclose or make obvious the particular combination of elements which comprise Applicant's invention. It is respectfully requested, therefore, that the Examiner reconsider and withdraw the above rejections under 35 U.S.C. § 102(b) and/or 103(a) to the Applicant's claims.

In view of the foregoing, Applicants respectfully assert that claims 7-14 and 17-22 are in condition for immediate allowance. In the event that Examiner finds any remaining impediments to the prompt allowance of any of these claims which could be clarified by telephone conference, Examiner is respectfully urged to initiate the same with the undersigned.

DATED this 14th day of July, 2003.

Respectfully submitted,

Gary D. E. Pierce
Attorney for Applicant
Registration No. 38,019

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PATE PIERCE & BAIRD
550 Parkside Tower
215 South State Street
Salt Lake City, Utah 84111
Telephone: (801) 530-0330
Facsimile: (801) 530-5955